CHAPTER X: FUNCTIONAL MAGNETIC RESONANCE IMAGING

Now let me give a very brief background in functional magnetic resonance imaging if there are any left in this audience that may be unfamiliar with it. Unlike say EEG and MEG, where we're directly measuring electrical activity, in functional magnetic resonance today, we don't yet understand the trick that will I hope ultimately be discovered that will allow us to directly measure electrical activity, so we have to indirectly infer electrical activity through direct measures of other physiological changes that are occurring in the brain.

There are a wide variety of different tools that we use that kind of fall under this general category of functional MRI. The most common in human studies is the so-called bold effect; I'll talk about that in a little bit. There are other techniques that allow us to directly measure blood flow or blood volume. Because it turns out that when the brain is active, all of these hemodynamic physiological changes occur locally and in concordance with the underlying brain activity, so for example, relative to a resting state, when a part of your brain is active, if your visual cortex is looking at this slide, auditory cortex listening to my voice, perhaps your sleep centers firing if you were out late in the lab last night or someplace else.

And you know, there's a whole host of areas that are -- a whole host of physiological changes that are occurring, including increases in blood flow, blood volume, increases in oxygen consumption, although somewhat paradoxically, but quite important for much of the functional imaging that we do, because the delivery of oxygen, the blood flow, outstrips the increase in utilization of oxygen, the oxygen content of the blood actually goes up. Deoxyhemoglobin, the hemoglobin where the blood has been stripped of its oxygen, actually goes down.

Well, what does this mean? It was actually Ken Kwong that was the first to show that just doing a series of images that were sensitive, could be made sensitive to these underlying physiological events; we could literally watch the brain turning on. This is a simple experiment where Ken simply put a subject in the magnet, we'll just run the loop one more time, there’s the baseline picture.

And then in a series of subtractions of subsequent images from that baseline, he was able to show directly the part of the brain that lit up, in this case with a visual stimulus, simple flashing checker boards, a quite remarkable finding both because of its power and its ability to localize brain activity and ultimately in its simplicity. Because in fact, without the required injection of any radioactive tracers or contrast media, essentially we could watch the changes in hemodynamics occur in real time.

The cascade of events that leads these physiological changes to the signal changes is actually an interesting one and the story is now, you know, more than a hundred years old in its full telling. It was more than a hundred years ago that **Angelo Mosso** and the English physiologists Roy and Sherrington showed that there were these physiological hemodynamic changes that occurred in the brain when the brain was more active and the great neurosurgeon, Wilder Penfield, who actually showed during surgery that the brain actually increased its oxygenated hemoglobin when the brain was stimulated, that was in the '30s.

Interestingly though, right around the same time, in 1930 Linus Pauling, the great protein chemist, showed that the magnetic properties of hemoglobin changed when it was oxygenated versus deoxygenated. And it was folks like Keith Thulborn initially in test tubes and Segi Ogawa in animal models who showed that that change in the magnetic property originally seen more than 60 years before could lead to signal changes on magnetic resonance images.

Putting it all together, Ken Kwong at the MGH back in 1991 was able to show that when the brain was active, there were these similar mechanisms in place in terms of biophysics of the MMR response and thus, we could directly see brain activity.